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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|------------------------|----------------------|------------------|
| 10/717,434 | 11/18/2003 | Charlotte Albaek Thrué | 58404 (71432) | 7602 |
| 21874 | 7590 | 11/03/2005 | EXAMINER | |
| EDWARDS & ANGELL, LLP P.O. BOX 55874 BOSTON, MA 02205 | | | VIVLEMORE, TRACY ANN | |
| | | ART UNIT | PAPER NUMBER | 1635 |

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|-----------------------------|------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 10/717,434 | THRUE ET AL. |
| | Examiner Tracy Vivlemore | Art Unit 1635 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on _____.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-4, 10-12, 22-24, 32-34 and 39-41 is/are rejected.
- 7) Claim(s) 5-9, 13-21, 25-31, 35-38 and 42 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 18 November 2003 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>7/04 and 11/04</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Claim Objections

Claims 5-9, 13-21, 25-31, 35-38 and 42 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim 10, 24, 33 and 40 are objected to because of the following informalities: claim 10 refers to sequences V and Y while the letters are defined as representing single nucleotide units. The word "length" is misspelled in the next to last line of claim 24 and in lines 6 and 8 of claim 33. Claim 33 recites that it depends from "any of claims 32" while claim 40 recites that it depends from "any of claims 39". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is directed to a pharmaceutical composition and is indefinite because a proper composition claim must contain at least two different elements. Claim 1 contains only one element, the antisense oligonucleotide construct. Claims 2-4 are indefinite due to their dependence from claim 1.

Claims 2-4, 11, 12, 22-24, 32-34 and 39-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrases in these claims, including "such as" and "preferably", render the claim indefinite because it is unclear whether the phrases in parentheses and the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim recites that the sequence represented by B is "optionally spiked with an other nucleotide". The word "spiked" is not a term of art and

is undefined in the specification, thus it is unknown what this term refers to in the context of a nucleotide sequence.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 10-12, 32 and 39-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Wahlestedt et al. (WO 01/25248, cited on IDS).

Claims 1-3, 10-12, 32 and 39-41 are directed to oligonucleotides that comprises at least one amino- or thio-LNA or at least two alpha-L-oxy-LNA, further comprising ribose or erythrose nucleotides and additional locked nucleotides and may contain modified internucleotide linkages. Claim 32 is directed to an oligonucleotide having a particular pattern of locked and non-locked nucleotide units.

Wahlestedt et al. disclose antisense oligonucleotides having LNA and non-LNA segments. LNAs include oxy-LNA, thio-LNA and amino-LNA. Non-LNA sequences are disclosed as comprising DNA and RNA and analogues. Page 8 describes that the oligonucleotides of the invention comprise patterns of alternating locked and non-locked nucleotides of varying lengths, including those in claim 24, that may comprise internucleotide linkages such as phosphorothioates.

Thus, Wahlestedt et al. disclose all limitations of and anticipate claims 1-3, 10-12, 32 and 39-41.

Claims 1-4, 10-12, 22, 23 and 39-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Orum et al. (WO 01/48190, cited on IDS).

Claims 1-4, 10-12, 22, 23 and 39-41 are directed to oligonucleotides that comprises at least one amino- or thio-LNA or at least two alpha-L-oxy-LNA, further comprising ribose or erythrose nucleotides and additional locked nucleotides and may contain modified internucleotide linkages.

Orum et al. disclose antisense oligonucleotides having LNA and non-LNA segments. LNA monomers are disclosed on page 5 as including oxy-LNA, thio-LNA and amino-LNA and can be connected by phosphorothioate linkages. α -LNA is disclosed on page 10. Non-LNA sequences are disclosed as comprising DNA and RNA and analogues. Orum et al. disclose on page 36 a sequence designated as Cur0102 that meets the length limitations of claim 24.

Thus, Orum et al. disclose all limitations of and anticipate claims 1-4, 10-12, 22, 23 and 39-41.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 10-12, 32-34 and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wahlestedt et al.

Claims 1-3, 10-12, 32 and 39-41 are described in the 102 rejection over Wahlestedt et al. Claims 33 and 34 depend from claim 32 and are directed to a pattern of locked and non-locked nucleotide sequences reciting specific lengths of each segment.

Wahlestedt et al. teach oligonucleotides comprising locked and non-locked nucleotides and disclose one particular sequence that comprises the pattern shown in claim 32. Wahlestedt et al. do not teach sequences having the specific lengths recited in claims 33 and 34.

One of ordinary skill in the art would be motivated to modify the invention of Wahlestedt et al. to produce antisense oligonucleotides wherein the individual segments have particular lengths in order to produce an antisense oligonucleotide having the

necessary degree of specificity and stability suitable for their particular application.

MPEP section 2144.05 describes that routine optimization or experimentation of what is known in the prior art supports a *prima facie* case of obviousness. One of ordinary skill in the art would have had a reasonable expectation of success in producing antisense oligonucleotides having the specific lengths recited in the instant claims because it is routine in the art of nucleic acid synthesis to produce oligonucleotides of any desired sequence length and configuration.

Thus, the invention of claims 1-3, 10-12, 32-34 and 39-41 would have been obvious, as a whole, at the time of invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your

application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
October 19, 2005


**J.D. SCHULTZ, Ph.D.
PATENT EXAMINER**